AMENDMENTS TO THE CLAIMS

This listing of Claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1. (Withdrawn) A method for identifying a compound which modulates the activation or phosphorylation of an AMP-activated protein kinase or an AMP-activated protein kinase subfamily member in a cell, the method comprising the steps of (1) determining whether a test compound modulates the protein kinase activity of LKB1 and (2) selecting a compound which modulates the protein kinase activity of LKB1, wherein the LKB1 is in a preparation comprising STRAD or MO25 or both.

2. (Withdrawn) The method of claim 1 wherein the LKB1, STRAD or MO25 is recombinant and is expressed from a recombinant nucleic acid.

3. (Currently Amended) A preparation comprising at least 30% by weight of a complex of an LKB1 polypeptide, a STRAD polypeptide and a recombinant MO25 polypeptide expressed from a recombinant nucleic acid, wherein:
   (a) said LKB1 polypeptide phosphorylates or activates an AMPK comprising a amino acid sequence having at least 90% homology to the residues 1-19 of SEQ ID NO: 110 in a T-loop binding domain and capable of binding LKB1, and the LKB1 comprises a catalytically active domain ~~comprising~~ having at least 90% sequence homology with ~~at least one of:~~ residues 44-343 of SEQ ID NO: 6~~, a variant thereof having a conservative substitution, and a variant thereof having at least 65% sequence homology~~;
   (b) said STRAD polypeptide binds to said LKB1, said STRAD polypeptide binds to [[and]] MO25, and comprises a polypeptide having at least 90% homology to at least one of SEQ ID NO: 9 or SEQ ID NO: 10, and comprises a ~~C~~

~~terminal pseudokinase domain, said C-terminal pseudokinase domain comprising the~~ C-terminal sequence Trp-Glu-Phe; and

(c) said MO25 binds to STRAD, and comprises a sequence having at least 90% sequence homology with at least one of ~~selected from the group consisting of:~~ SEQ ID NO: 11, SEQ ID NO: 22 [[12]], SEQ ID NO: 13, SEQ ID NO: 159 [[14]], or SEQ ID NO: 15~~, a variant of any of the foregoing having a conservative substitution, and a variant of any of the foregoing having at least 65% sequence homology~~.

4. (Previously Presented) The preparation of claim 3 comprising recombinant LKB1 expressed from a recombinant nucleic acid.

5. (Previously Presented) The preparation of claim 4 comprising recombinant STRAD expressed from a recombinant nucleic acid.

6. (Withdrawn) A cell capable of expressing LKB1, STRAD and overexpressed or recombinant MO25 expressed from a recombinant nucleic acid.

7. (Withdrawn) The cell of claim 6 comprising a recombinant nucleic acid encoding MO25.

8. (Withdrawn) The cell of claim 7 comprising a recombinant nucleic acid encoding LKB1.

9. (Withdrawn) The cell of claim 8 comprising a recombinant nucleic acid encoding STRAD.

10. (Withdrawn) A cell comprising LKB1, STRAD and overexpressed or recombinant MO25 expressed from a recombinant nucleic acid.

11. (Withdrawn) A cell according to claim 10 comprising recombinant LKB1 expressed from a recombinant nucleic acid.

12. (Withdrawn) A cell according to claim 10 comprising recombinant STRAD expressed from a recombinant nucleic acid.

13. (Canceled)

14. (Withdrawn) A method for making a purified preparation comprising LKB1, STRAD and recombinant MO25 expressed from a recombinant nucleic acid comprising: selecting a cell according to claim 10 and purifying the preparation from the cell.

15. (Canceled)

16. (Cancelled)

17. (Canceled)

18. (Canceled)

19. (Currently Amended) [[A]] An *in vitro* method for identifying a compound for modulating ~~cellular~~ LKB1 activity, the method comprising the steps of:

(a) contacting a substrate polypeptide with a LKB1-STRAD-MO25 complex, wherein

(i) the substrate polypeptide comprises myelin basic protein or comprises a sequence of at least 90% homology to at least one of ~~selected from the group consisting of~~: SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, or SEQ ID NO: 110~~, a variant thereof having a~~

~~conservative substitution, and a variant thereof having at least 65% sequence homology~~;

(ii) the LKB1-STRAD-MO25 complex comprises:

(A) an LKB1 polypeptide that phosphorylates or activates an AMPK comprising a amino acid sequence having at least 90% homology to the residues 1-19 of SEQ ID NO: 110 in a T-loop binding domain and capable of binding LKB1, and comprises a catalytically active domain having at least 90% sequence homology with ~~comprising at least one of~~: residues 44-343 of SEQ ID NO: 6~~, a variant thereof having a conservative substitution, and a variant thereof having at least 65% sequence homology~~;

(B) a STRAD polypeptide that binds to said LKB1, [[and]] binds to MO25, and comprises a polypeptide having at least 90% homology to at least one of SEQ ID NO:9 or SEQ ID NO: 10, and comprises a ~~C-terminal pseudokinase domain, said C-terminal pseudokinase domain comprising the~~ C-terminal sequence Trp-Glu-Phe; and

(C) a MO25 polypeptide that binds to STRAD, and comprises a sequence having at least 90% sequence homology with at least one of ~~selected from the group consisting of~~: SEQ ID NO: 11, SEQ ID NO: 22 [[12]], SEQ ID NO: 13, SEQ ID NO: 159 [[14]], and SEQ ID NO: 15~~, a variant of any of the foregoing having a conservative substitution, and a variant of any of the foregoing having at least 65% sequence homology~~; [[and]]

(b) measuring the phosphorylation of the substrate peptide and

(c) concluding that the compound modulates LKB1 activity if the measured phosphorylation of the substrate peptide is significantly increased or decreased in the presence of the compound.

20. (Previously Presented) The method of claim 19 wherein the LKB1 protein kinase activity is measured using an AMPK or an AMPK subfamily member or a fragment thereof as a substrate.

21. (Withdrawn) A kit of parts comprising the preparation of claim 3.

22. (Withdrawn) A kit of parts according to claim 21 further comprising (1) an AMPK or an AMPK subfamily member, or recombinant polynucleotide encoding AMPK or AMPK subfamily member or a fragment thereof.

23. (Withdrawn) A method for overexpressing LKB1 comprising the steps of (1) selecting a cell according to claim 6 in which to overexpress LKB1 and (2) overexpressing LKB1 in the selected cell.

24. (Withdrawn) A method according to claim 23 further comprising preparing LKB1 from the cell.

25. (Withdrawn) A method for identifying a putative binding partner for MO25 comprising the steps of (1) providing an amino acid sequence of at least the C-terminal three amino acids of a test putative binding partner (2) selecting a putative binding partner having the C-terminal amino acid sequence Trp-Glu/Asp-Phe.

26. (Withdrawn) The method of claim 25 further comprising the step of determining that the selected putative binding partner binds to MO25.

27. (Withdrawn) A method for identifying a genetic difference associated with PJS (Peutz-Jeghers Syndrome) comprising the steps of (1) investigating the sequence of a gene encoding a MO25 isoform in at least one patient having PJS (2) identifying any difference between the said patient sequence and equivalent sequence from an individual without PJS.

28. (Withdrawn) A method for determining whether an individual is susceptible to PJS comprising the steps of determining whether the test individual has a genetic difference identified as associated with PJS by a method according to claim 27.

29. (Withdrawn) A method for identifying a compound which activates an AMPK or an AMPK subfamily member by a similar mechanism to metformin or phenformin or AICA riboside comprising comparing the effect of a test compound on the activation of the AMPK or the AMPK subfamily member by a preparation according to claim 3 with the effect of metformin or phenformin or AICA riboside on the activation of the AMPK or the AMPK subfamily member and selecting the compound with a similar effect.

30. (Canceled)

31. (Withdrawn) The kit of parts of claim 22 wherein the AMPK subfamily member is or comprises an AMPKα1 or AMPKα2 polypeptide.

32. (Withdrawn) The kit of parts of claim 22 wherein the AMPK subfamily member is or comprises a NUAK1, NUAK2, BRSK1, BRSK2, SIK, QIK, QSK, MARK1, MARK2, MARK3, MARK4 or MELK polypeptide.

33. (Withdrawn) A peptide substrate for LKB1 comprising the amino acid sequence SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, LSNLYHQGKFLQTFCGSPLY (SEQ ID NO:16), FGNFYKSGEPLSTWCGSPPY (SEQ ID NO:17), LSNMMSDGEFLRTSCGSPNY (SEQ ID NO:18), MASLQVGDSLLETSCGSPHY (SEQ ID NO:19), FSNEFTVGGKLDTFCGSPPY (SEQ ID NO:20), or AKPKGNKDYHLQTCCGSLAY (SEQ ID NO:21); or said amino acid sequence with from one to four substitutions therein at any position other than the underlined residue and/or a conservative substitution at the underlined residue; or at least ten contiguous residues of said sequence encompassing the underlined residue.

34. (Withdrawn) A peptide substrate for LKB1 according to claim 1 consisting of the amino acid sequence LSNLYHQGKFLQTFCGSPLY (SEQ ID NO:16),

LSNLYHQGKFLQTFCGSPLYRRR (SEQ ID NO:23), SNLYHQGKFLQTFCGSPLY SEQ ID NO:24), SNLYHQGKFLQTFCGSPLYRRR (SEQ ID NO:25), FGNFYKSGEPLSTWCGSPPY (SEQ ID NO:17), FGNFYKSGEPLSTWCGSPPYRRR (SEQ ID NO:29), LSNMMSDGEFLRTSCGSPNY (SEQ ID NO:18), LSNMMSDGEFLRTSCGSPNYRRR (SEQ ID NO:31), MASLQVGDSLLETSCGSPHY (SEQ ID NO: 19), MASLQVGDSLLETSCGSPHYRRR (SEQ ID NO:33), or FSNEFTVGGKLDTFCGSPPY (SEQ ID NO: 20), FSNEFTVGGKLDTFCGSPPYRRR (SEQ ID NO: 35), AKPKGNKDYHLQTCCGSLAY (SEQ ID NO: 21), or AKPKGNKDYHLQTCCGSLAYRRR (SEQ ID NO: 37).

35. (Withdrawn) An antibody reactive with a peptide antigen having the amino acid sequence MVAGLTLGKGPESPDGDVS (SEQ ID NO: 38) (residues 1-20 of human BRSK1), LSWGAGLKGQKVATSYESSL (SEQ ID NO: 39) (residues 655-674 of human BRSK2), MEGAAAPVAGDRPDLGLGAPG (SEQ ID NO: 40) (residues 1-21 of human NUAK1), TDCQEVTATYRQALRVCSKLT (SEQ ID NO: 41) (residues 653-673 of human NUAK2), MVMADGPRHLQRGPVRVGFYD (SEQ ID NO: 42) (residues 1-21 of human QIK), MVIMSEFSADPAGQGQGQQK (SEQ ID NO: 43) (residues 1-20 of human SIK), GDCEMEDLMPCSLGTFVLVQ (SEQ ID NO: 44) (residues 765-784 of human SIK), TDILLSYKHPEVSFSMEQAGV (SEQ ID NO: 45) (residues 1349-1369 of human QSK), SGTSIAFKNIASKIANELKL (SEQ ID NO: 46) (residues 776-795 of human MARK1), MSSRTVLAPGNDRNSDTHGT (SEQ ID NO: 47) (residues 1-20 of human MARK4), MKDYDELLKYYELHETIGTG (SEQ ID NO: 48) (residues 1-20 of human MELK), CTSPPDSFLDDHHLTR (SEQ ID NO: 49) (residues 344-358 of rat AMPKα1), CDPMKRATIKDIRE (SEQ ID NO: 50) (residues 252 to 264 of rat AMPKα1).